

Please amend the application as follows:

In the Claims

Please cancel Claims 26, 28, 48, 54, 56, and 58.

Please amend Claims 27, 29, 30, 32, 33, 43, 45, 52, 57, 69, 70, 72, 73 and 76.

Amendments to the claims are indicated in the attached "Marked Up Version of Amendments" (pages i - ii).

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C1 27. (Amended) The method of Claim 33 wherein gene expression is localized to the sinoatrial node region of the right atria.

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C2 29. (Twice Amended) The method of Claim 33 wherein gene expression is regulated by at least one expression control element.

30. (Amended) The method of Claim 29 wherein the expression control element directs transient expression.

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C3 32. The method of Claim 33 wherein the cell is isogenic, allogenic, or xenogenic.

33. (Amended) A method of upregulating heart rate in a mammal by introducing a modified cell transfected or transduced with at least one gene that upregulates heart rate, said gene selected from the group consisting of:  $\beta_2$ AR,  $\beta_1$ AR and  $G_{\alpha s}$ , into the sinoatrial node region of a mammalian heart, wherein the introduced cells express the gene in the cardiac tissue of the mammal resulting in an upregulated heart rate.

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C4 43. (Amended) The method of Claim 29 wherein the expression control element directs stable expression.

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C5 45. (Amended) The method of Claim 43 wherein the expression control element comprises an inducible promoter.

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C6 52. (Twice Amended) The method of Claim 33 wherein the transfected or transduced modified cell expressing a  $\beta_2$ -adrenergic receptor further comprises *in vivo* administration of an adrenergic agonist.

C7 57. (Amended) The method of Claim 33 wherein the modified cell is selected from the group consisting of: a myoblast, a cardiomyocyte, a skeletal muscle myoblast, a fetal or embryonic cardiomyocyte and a cardiac-derived cell line.

C8 69. (Amended) A method of permanently upregulating heart rate in a mammal by introducing at least one fetal or embryonic cardiomyocyte transfected or transduced with at least one gene that upregulates heart rate, said gene selected from the group consisting of:  $\beta_2$ AR,  $\beta_1$ AR and  $G_{as}$ .

70. (Twice Amended) A method of upregulating heart rate in a mammal by introducing a construct comprising at least one gene selected from the group consisting of:  $\beta_2$ AR,  $\beta_1$ AR and  $G_{as}$ , wherein said construct is suitable for localized stable gene expression in mammalian cardiac atrial tissue, and wherein said construct is introduced by direct myocardial injection or endocardiac transfection or transduction.

C9 72. (Amended) The method of Claim 70, wherein the construct is introduced into the sinoatrial node region of a mammalian heart.

73. (Amended) The method of Claim 70, wherein the method further comprises *in vivo* administration of an adrenergic agonist.

C10 76. (Amended) A cell in culture transduced or transfected with at least one gene that increases the rate of contraction of the cell.

Please add new Claims 78-86 shown below.

C11 78. (New) A method of altering cardiac rhythm in a mammal by introducing a modified cell transfected or transduced with at least one gene that upregulates heart rate, said gene selected from the group consisting of:  $\beta_2$ AR,  $\beta_1$ AR and  $G_{as}$ , into the sinoatrial node region

of a mammalian heart, wherein the cells express the gene in the cardiac tissue of the mammal resulting in an upregulated heart rate.

79. (New) The method of Claim 78 wherein gene expression is localized to the sinoatrial node region of the right atria.
80. (New) The method of Claim 78 wherein gene expression is regulated by at least one expression control element
81. (New) The method of Claim 80 wherein the expression control element directs transient expression.
82. (New) The method of Claim 80 wherein the expression control element directs stable expression.
83. (New) The method of Claim 82 wherein the expression control element comprises an inducible promoter.
84. (New) The method of Claim 78 wherein the cell is isogenic, allogenic, or xenogenic.
85. (New) The method of Claim 78 wherein the transfected or transduced modified cell expressing a  $\beta$ 2-adrenergic receptor further comprises *in vivo* administration of an adrenergic agonist.
86. (New) The method of Claim 78 wherein the modified cell is selected from the group consisting of: a myoblast, a cardiomyocyte, a skeletal muscle myoblast, a fetal or embryonic cardiomyocyte and a cardiac-derived cell line.

#### REMARKS

Applicants have canceled Claims 26, 28, 48, 54, 56, and 58. Applicants have amended Claims 27, 29, 30, 32, 33, 43, 45, 52, 57, 69, 70, 72, 73 and 76, and added new Claims 78-86. Applicants note that Claims 53, 71, 74, 75 and 77 depend on Claims amended herein. No new matter has been added. Entry of amended and new claims is respectfully requested.